K072631

510(k) Summary

510(k) Summary
Idaho Technology Inc. JBAIDS Plague Detection Kit

Introduction: According to the requirements of 21 CFR 807.92, the following information provides sufficient detail to understand the basis for a determination of substantial equivalence.

Submitted by: Idaho Technology Inc.
390 Wakara Way
Salt Lake City, UT 84108

Telephone: 801-736-6354
Facsimile: 801-588-0507

Contact Person: Beth Lingenfelter, ext. 407

DEC 2 0 2007

Date Prepared: September 14, 2007

Device Name: Trade Name: JBAIDS Plague Detection Kit

Common Name:

Real-time PCR assay for targeted *Yersinia pestis* DNA sequences

Classification Name:

Reagent Kit: *Y. pestis* DNA reagents (Unclassified)

Device Description: The Joint Biological Agent Identification and Diagnostic System (JBAIDS) Plague Detection Kit is a real-time polymerase chain reaction (PCR) reagent kit, which, when used with the JBAIDS instrument and software, allows the qualitative *in vitro* diagnostic (IVD) detection of target DNA sequences within the pathogenic bacterium, *Yersinia pestis*, the causative agent of plague. The kit contains two assays, Plague Target 1 and Target 2, each of which consists of oligonucleotide primers and a fluorescent-labeled target assay probe that specifically detect *Y. pestis* DNA. The Target 2 assay is reserved for samples that test positive with the Target 1 assay. The kit is designed for use with the JBAIDS instrument, a portable thermocycler and real-time fluorimeter that performs PCR in glass capillaries.

Before testing, samples are purified using Idaho Technology's 1-2-3™ Sample Purification Kits (or validated equivalent). The resulting purified sample is added to an Unknown reagent vial and an Inhibition Control reagent vial, along with reconstitution buffer. When the organism is present, a fragment of *Y. pestis* DNA is amplified. The amplicon is detected by fluorescence using a specific hydrolysis

probe. The hydrolysis probe contains a short oligonucleotide that hybridizes to an internal sequence of the amplified fragment during the annealing phase of the PCR cycle. This probe has the 5' and 3' ends labeled with a reporter dye and a quenching dye, respectively. When the probe hybridizes to the specific DNA target, the Taq polymerase enzyme replicating the target-specific DNA hydrolyzes the probe, separating the two fluorophores and allowing the reporter dye to fluoresce.

The JBAIDS instrument measures the level of fluorescence from each unknown sample and control. JBAIDS Software analyzes the fluorescence amplification curves and reports results as positive, negative, inhibited, or uncertain. A failure of the Positive or Negative Control will result in the entire run being called invalid. Failure of the Inhibition Control yields an inhibited result when the associated sample has a negative result for the target assay and requires retesting of that sample.

Intended Use: The Joint Biological Agent Identification and Diagnostic System (JBAIDS) Plague Detection Kit is a real-time polymerase chain reaction (PCR) test kit intended for the qualitative *in vitro* diagnostic (IVD) detection of target DNA sequences of *Yersinia pestis*. The kit can be used to test human whole blood collected in sodium citrate or sputum collected aseptically from individuals greater than 18 years of age suspected of having septic or pneumonic plague. In addition, positive blood cultures and colonies may be tested. The JBAIDS Plague Target 2 assay is used as a supplementary test only after a positive result with the Target 1 Assay.

The JBAIDS Plague Target 1 and Target 2 assays are run on the JBAIDS instrument using the Diagnostic Wizard. Results are for the presumptive identification of *Y. pestis* in conjunction with culture and other laboratory tests. The definitive identification of *Y. pestis* from colony growth, liquid blood culture growth, or from blood or sputum specimens requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reports are required.

The diagnosis of plague must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence in addition to the identification of *Y. pestis* from cultures or directly from whole blood or sputum specimens.

The JBAIDS Plague Detection Kit is intended for use by trained clinical laboratory personnel who have received specific training on the use of the JBAIDS Plague Detection Kit. The level of *Y. pestis* that would be present in blood or sputum from individuals with early systemic infection is unknown. Due to the difficulty in obtaining clinical specimens, these assays were not evaluated with blood or sputum from individuals with septic or pneumonic plague.

Substantial Equivalence: The JBAIDS Plague Detection Kit is substantially equivalent to direct immunofluorescence assays (DFA) using fluorescein-labeled antibodies against the Fraction 1 (F1) capsular antigen of *Y. pestis*. This preamendment device was considered at the FDA's Microbiology Devices Advisory Panel meeting on March 7, 2002 and was determined to be a Class II device.

JBAIDS Plague Detection Kit vs. Fluorescein-labeled antibody to F1 antigen

ELEMENT	JBAIDS Plague Detection Kit	DFA using a Fluorescein-labeled antibody to F1 capsular antigen (Preamendment)
Intended Use	Qualitative detection of *Y. pestis*.	Same
Indications for Use	Identification of *Y. pestis* in individuals suspected of having septic or pneumonic plague.	Identification of *Y. pestis* in individuals suspected of having septic, pneumonic or bubonic plague.
Technological Principles	Real-time PCR using hydrolysis probes.	Microscopic visualization of *Y. pestis* bacteria via specific binding of a fluorescently labeled antibody.
Assay Target	DNA sequences unique to *Y. pestis*	F1 antigen
Specimen Types	Whole blood (collected in 3.2% sodium citrate), sputum, blood culture or bacterial colonies.	Whole blood, sputum, CSF, bubo aspirates, skin lesion scrapings and bacterial cultures, or blood culture media in which gram-negative organisms can be seen.
Instrumentation	JBAIDS instrument (K051713)	Fluorescent microscope
Time Required for Analysis of Specimen	Less than 3 hours	Same
Test Interpretation	Automated test interpretation and report generation.	Subjective interpretation by user.
Physical Properties	Freeze dried reagents with reconstitution buffer and water provided in kit.	Liquid reagent
Storage and Shelf Life	One year at room temperature (18–28 °C).	Refrigerator temperature (2–8 °C), manufacture defined expiration date.

The predicate device and the JBAIDS Plague Detection Kit have the same intended use. Both provide test results that aid in the diagnosis of plague when considered with other clinical and microbiological evidence, both test for *Y. pestis* infection directly from patient specimens or cultures, and both provide qualitative test results.

While the basic intended use is the same for the predicate device and the JBAIDS Kit, the technological characteristics are quite different. The sensitivity and specificity of DFA assays rely on the titer and specificity of the labeled antibody. Because there are no specific test kits available, each laboratory develops its own assay using different antibodies. Further, the antibodies are sold as 'research use only' reagents, so the manufacturers do not supply performance data with regard to detection of *Y. pestis*. As a result, the safety and efficacy of the predicate test is largely unknown, although some literature exists that can aid in comparing the two devices.

In a recent study, Tomaso et al. evaluated the analytic performance of several different immunologic methods, including ELISA, flow cytometry and DFA, for the detection of the F1 capsular antigen.[1] The lower limit of detection (LOD) for DFA was 10^3 CFU/mL of *Y. pestis* in phosphate buffered saline (PBS) when using a monoclonal antibody labeled with OregonGreen™. In the same study, this assay demonstrated 100% (10/10)

inclusivity by detecting all isolates of *Y. pestis* tested and 100% (45/45) exclusivity by giving negative results for all other bacteria, including 10 non-*pestis Yersinia* species.

In contrast to the predicate, the sensitivity and specificity of the JBAIDS Plague Detection Kit relies on adequate recovery and purification of nucleic acids from patient specimens and on the specificity of the PCR primers and probes. The LOD for the JBAIDS Plague Detection System is 50 CFU/mL of citrated whole blood and 670 CFU/mL of sputum.

The analytic sensitivity, or inclusivity, of the JBAIDS Plague Detection Kit was determined by testing colonies and purified DNA from various subtypes and strains of *Y. pestis*. Given the plasmid status of the tested strains, all 18 (100%) isolates of virulent *Y. pestis* tested with the JBAIDS Plague Detection System gave the expected test result. Fifteen (83%) would have been considered presumptively positive for *Y. pestis* because they were detected by both assays. Two isolates would have given an indeterminate result because they are missing the gene target for the Target 2 assay while, one isolate would have tested false negative because it is missing the gene target for the Target 1 assay.

Analytic specificity, or exclusivity, of the JBAIDS Plague Detection System was determined by testing panels containing organisms that are phylogenetically related to *Y. pestis* (nearest neighbors), as well as unrelated organisms that are likely to be found in clinical samples. The JBAIDS Target 1 assay gave negative results for 100% (24/24) of the tested isolates; however, uncertain results were sometimes obtained when testing one of three isolates of *Y. enterocolitica* with the Target 2 assay. As the result for Target 1 was negative when testing this strain, Target 2 would not be tested and a false positive result would not be obtained. These data support that the overall analytic specificity for the JBAIDS Plague Detection Kit is high and equivalent to the predicate.

In addition to analytic studies, a multisite clinical trial was conducted. Due to the near absence of clinical samples from individuals with a diagnosis of systemic plague, the clinical trial was limited to an assessment of the system's clinical specificity. Blood and/or sputum samples obtained from subjects with clinical signs and symptoms consistent with systemic plague and for whom a blood and/or sputum culture had been ordered were tested for *Y. pestis* using both assays of the JBAIDS Plague Detection Kit. The results were compared to the laboratory culture results, which were considered the gold standard. As expected, *Y. pestis* was not identified in any of the blood or sputum cultures. All 132 whole blood samples yielded negative test results with the Target 1 assay; however, two (1.5%) whole blood samples gave false positive results when tested with the Target 2 assay due to non-specific amplification that occasionally affects this assay. As the standard testing procedure is to reserve the Target 2 assay for use with samples that tested positive with Target 1 and all whole blood samples provided the correct negative test result with Target 1, the clinical specificity of the JBAIDS Plague Detection Kit is at least 97% (95% CI, 97-100%) for whole blood samples. All 36 (100%) sputum samples yielded negative results for both assays resulting in a clinical specificity of at least 92% (95% CI, 92-100%) for sputum.

Based on the available literature, the JBAIDS Plague Detection Kit appears to be as safe and effective as the predicate assay. A positive result with either DFA or the JBAIDS Plague Detection Kit provides presumptive identification of *Y. pestis*. Both tests have a high sensitivity and high specificity. However, the JBAIDS offers some advantages over the predicate. DFA tests can be difficult to interpret and require subjective evaluation. In

addition, the F1 capsular antigen is only formed when the organism is grown at or near body temperature.[2] Storage and transport of samples can result in loss of the F1 antigen and a false negative test result. In contrast, the JBAIDS software automatically interprets the assay results, reducing the opportunity for user error and the freeze-dried assay format minimizes assay setup errors. The JBAIDS Plague Detection Kit could identify infected individuals days before DFA, reducing the time to treatment and limiting person-to-person spread of the disease.

In summary, the JBAIDS assay, while technologically distinct from the predicate, is as safe and effective as the predicate, but could provide a more rapid diagnosis.

References

1. Tomaso H, Thullier P, Seibold E, et al. Comparison of hand-held test kits, immunofluorescence microscopy, ELISA, and flow cytometric analysis for the rapid presumptive identification of *Yersinia pestis*. *J. Clin. Microbiol.* 2007; doi:10.1128/JCM.00458-07
2. Perry RD, Fetherstone JD. *Yersinia pestis* – etiologic agent of plague. *Clin Microbiol Rev.* 1997;10:35-66.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

DEC 2 0 2007

Ms. Beth Lingenfelter
Manager, Regulatory Affairs
Idaho Technology, Inc
390 Wakara Way
Salt Lake City, UT 84108

Re: K072631
Trade/Device Name: JBAIDS Plague Detection Kit
Regulation Number: Unclassified
Product Code: NHT
Dated: December 17, 2007
Received: December 18, 2007

Dear Ms Lingenfelter:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in Title 21, Code of Federal Regulations (CFR), Parts 800 to 895. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); and good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820).

This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to a legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific information about the application of labeling requirements to your device, or questions on the promotion and advertising of your device, please contact the Office of *In Vitro* Diagnostic Device Evaluation and Safety at (240)276-0484. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address http://www.fda.gov/cdrh/industry/support/index.html

Sincerely yours,

Sally A. Hojvat, M.Sc., Ph.D.
Director
Division of Microbiology Devices
Office of *In Vitro* Diagnostic Device
Evaluation and Safety
Center for Devices and
Radiological Health

Enclosure

Indications for Use

510(k) Number (if known): K072631

Device Name: JBAIDS Plague Detection Kit

Indications for Use:

The Joint Biological Agent Identification and Diagnostic System (JBAIDS) Plague Detection Kit is a real-time polymerase chain reaction (PCR) test kit intended for the qualitative *in vitro* diagnostic (IVD) detection of target DNA sequences of *Yersinia pestis*. The kit can be used to test human whole blood collected in sodium citrate or sputum collected aseptically from individuals greater than 18 years of age suspected of having septic or pneumonic plague. In addition, positive blood cultures and colonies may be tested. The JBAIDS Plague Target 2 assay is used as a supplementary test only after a positive result with the Target 1 Assay.

The JBAIDS Plague Target 1 and Target 2 assays are run on the JBAIDS instrument using the Diagnostic Wizard. Results are for the presumptive identification of *Y. pestis* in conjunction with culture and other laboratory tests. The definitive identification of *Y. pestis* from colony growth, liquid blood culture growth, or from blood or sputum specimens requires additional testing and confirmation procedures in consultation with public health or other authorities for whom reports are required.

The diagnosis of plague must be made based on history, signs, symptoms, exposure likelihood, and other laboratory evidence in addition to the identification of *Y. pestis* from cultures or directly from whole blood or sputum specimens.

The JBAIDS Plague Detection Kit is intended for use by trained clinical laboratory personnel who have received specific training on the use of the JBAIDS Plague Detection Kit. The level of *Y. pestis* that would be present in blood or sputum from individuals with early systemic infection is unknown. Due to the difficulty in obtaining clinical specimens, these assays were not evaluated with blood or sputum from individuals with septic or pneumonic plague.

Prescription Use ___X___ (Part 21 CFR 801 Subpart D) AND/OR Over-The-Counter Use _____ (21 CFR 801 Subpart C)

(PLEASE DO NOT WRITE BELOW THIS LINE-CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K072631